**DE NOVO CLASSIFICATION REQUEST FOR**
**MATRx plus**

## REGULATORY INFORMATION

FDA identifies this generic type of device as:

**Auto titration device for oral appliances:** An auto-titration device for oral appliances is a prescription home use device that determines a target position to be used for a final oral appliance for the reduction of snoring and mild to moderate obstructive sleep apnea.

**NEW REGULATION NUMBER:** 21 CFR 872.5571

**CLASSIFICATION:** Class II

**PRODUCT CODE:** QCJ

## BACKGROUND

**DEVICE NAME:** MATRx plus

**SUBMISSION NUMBER:** DEN170090

**DATE OF DE NOVO:** December 21, 2017

**CONTACT:** Zephyr Sleep Technology
#102, 701 64th Ave SE
Calgary, Alberta Canada
T2H 2C3

## INDICATIONS FOR USE

The MATRx plus device may also be used with an automated mandibular positioner that uses feedback control to record changes in the patient's respiratory status related to repositioning of the mandible during an overnight study.

MATRx plus uses these recordings to produce a report for the HCP that can be used to prospectively identify patients with mild to moderate obstructive sleep apnea who may be suitable for therapy with an oral appliance and to recommend a target mandibular position.

The use of the device does not replace the need for follow-up testing to determine the initial and ongoing effectiveness of the therapy as recommended by clinical practice guidelines.

## LIMITATIONS

Prescription use only.

In an Oral Appliance Study mode, the device is not recommended for use in patients who:

- Have loose teeth or advanced periodontal disease
- Have full dentures or dental implants

This device is not to be used as an apnea monitor or in a life supporting or life sustaining situation.

## Warnings

Patients fitted with an oral appliance after their MATRx plus Study, as prescribed by the interpreting physician, should be monitored and undergo further sleep testing with their therapeutic appliance in place to ensure adequate treatment is achieved.

Use of the device during an Oral Appliance Study may cause:

- Temporary bite changes
- Gum or tooth discomfort
- Jaw discomfort
- Jaw joint discomfort
- Increased salivation
- Dry mouth

Use of the MATRx plus may cause disruption in sleep from the use of the sensors and mandibular positioner.

Inspect the titration trays and tray material carefully prior to each use. Stop the study and return the system to the provider if:

- The tray material has degraded
- The tray material has come off the Titration Trays during the study. If this occurs, remove any pieces from the mouth
- The titration trays are uncomfortable due to the tray material

Use of the titration trays is not to exceed 3 nights of sleep (total 24 hours).

PLEASE REFER TO THE LABELING FOR A MORE COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

## DEVICE DESCRIPTION

This De Novo request is for an expanded indication (new intended use) for use with an automated mandibular positioner that uses feedback control to record changes in the patient's respiratory status related to repositioning of the mandible during an overnight study.

The device is an automated temporary oral appliance that manipulates the mandible through multiple protrusion levels during an overnight sleep study in the home. The device uses the same interface as the MATRx plus Home Sleep Apnea Test, also from Zephyr Sleep Technologies, cleared under product code MNR, regulation 21 CFR 868.2375, cleared in K163665. These components include the recorder, tablet, oximeter, effector belt, and nasal cannula. The MATRx plus device for a titration study includes a mandibular positioner to determine an optimal titration position based on inputs of airflow and an oxygen desaturation index (ODI) of less than 10 events per hour. The device analyses the collected information and generates a report to assist the Healthcare Provider in the clinical management of oral appliance therapy for patients with mild to moderate obstructive sleep apnea. From this report, patients may be informed on the future efficaciousness of oral appliance (OA) therapy.

Specifically, the clinical management may be assisted by this type of oral appliance assessment study by prospectively identifying patients that are expected to achieve therapeutic success with oral appliance therapy. The oral appliance assessment study also includes the provision of a recommended target protrusive setting for the mandible through use of a legally marketed intraoral appliance (regulated under 21 CFR 872.5570, product code LQZ). The target protrusive setting is the amount of mandibular protrusion where the patient is expected to achieve efficacious therapy with the intraoral appliance and is used by the HCP to more effectively complete the titration process.

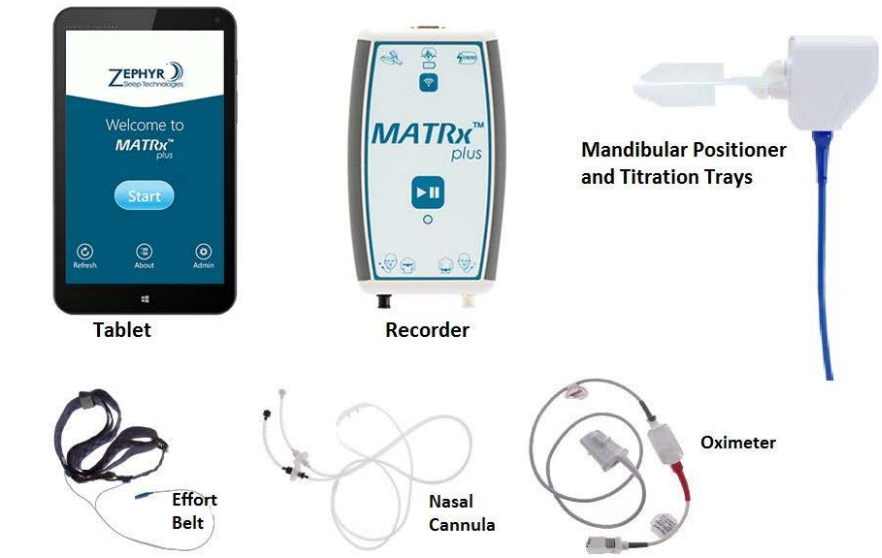
The use of the MATRx plus device for an oral appliance assessment study does not replace the clinical titration process or the need for follow-up testing to determine the initial and ongoing therapy as recommended by clinical practice guidelines.

The MATRx plus test identifies patients as suitable for intraoral therapy if a mandible protrusion level can be found where the patient has an oxygen desaturation index (ODI) of less than 10 events per hour with a 4% desaturation criterion.

Device Components

The components of the MATRx plus device for use in a titration study, are shown below in Figure 1:

*Figure 1: MATRx Plus Device Components*




The MATRx plus comprises the following components that were previously cleared under premarket notifications (510(k)s):

- Body Worn Recorder (with accelerometer sensor) [510(k) #K163665]
- Tablet computer that runs the MATRx plus Application [510(k) #K163665]
- Study Management and Review Software (Portal and Data Viewer) [510(k) #K163665]
- Nasal Cannula [510(k) #K163665]
- Respiratory Effort Belt [510(k) #K163665]
- Sleep Sense Impendence Belt [510(k) #K042253, not pictured in Figure 1]
- Oximeter Sensors [510(k) #K101896, K051212, K090662]
- Vinyl Polysiloxane 2 Component Vulcanizing System [K930248, not pictured in Figure 1]
- Titration Trays (same material as in K103704)
- Mandibular Positioner (similar to that cleared in K103704)

## SUMMARY OF NONCLINICAL/BENCH STUDIES

### BIOCOMPATIBILITY/MATERIALS

The MATRx plus Recorder, Tablet, Nasal Cannula, Respiratory Effort Belt and Finger Oximeter were previously cleared for the use of the MATRx plus device as a sleep recorder (K163665). There have been no changes to these devices, or their use (type or duration of contact) as part of this product. Biocompatibility for these components was demonstrated in 510(k) #K163665.

The MATRx plus Titration Tray and Impression material are of the same material and contact as the Titration Tray and Impression material for the in-lab version of the device (MATRx, K103704). Type and duration of contact remain the same (<24 hours). Biocompatibility for these components was demonstrated in 510(k) #K103704.

## SHELF LIFE/REPROCESSING/STERILITY

The MATRx plus device consists of the following components and accessories: a Tablet, a body worn Recorder with nylon strap, Nasal Cannula, Finger Oximeter, Effort Belt, a Mandibular Positioner and disposable Titration Trays. All components except for the Mandibular Positioner and Titration Trays are the same as were previously cleared for the use of the device to assist in the diagnosis of sleep disordered breathing in K163655. Cleaning and disinfection instructions were validated in that submission, and there have been no changes to these components since to necessitate additional validation.

The Mandibular Positioner is reused between patients, and is similar to the Positioner used for an OA assessment study in the sleep lab (K103704). It may become contaminated with body fluids (e.g. patient saliva) because of proximity to the patient, or be subject to contamination during use from contact with soiled hands of patients or the HCP. It therefore requires cleaning and low level disinfection between uses. New testing for the mandibular positioner was provided following the same validation plan as the previous components. Validated cleaning and disinfection instructions have been provided.

The Titration Trays are single patient use and are to be disposed of following the MATRx plus test.

## ELECTROMAGNETIC COMPATIBILITY, WIRELESS AND ELECTRICAL SAFETY

The MATRx plus was tested in accordance with the following consensus standards and conformed with IEC 60601-1-2:2014. The device passed the following electromagnetic compatibility (EMC) safety tests:

*Table 1: Electromagnetic Compatibility (EMC) Safety Tests*

| Phenomenon | Basic EMC Standard | Immunity test level |
|---|---|---|
| **Electrostatic Discharge** | IEC 61000-4-2 | +/-8kV contact, +/-2,4,6,8, 15kV air |
| **Radiated RF EM fields** | IEC 61000-4-3 | 10V/m, 80MHz-2.7GHz, 80% AM at 1kHz |
| **Proximity fields from RF wireless communications equipment** | IEC 61000-4-3 | As per Clause 8.10 of IEC 60601-1-2, see Table 2: Proximity Field Parameters |
| **EFT/Bursts** | IEC 61000-4-4 | +/-2kV, AC mains, +/-1kV, I/O ports |
| **Surges Line-Line** | IEC 61000-4-5 | ± 0.5 kV, ±1 kV |
| **Surges Line-Ground** | IEC 61000-4-5 | ± 0.5 kV, ±1 kV, ±2 kV |
| **Rated power frequency magnetic fields** | IEC 61000-4-8 | 30A/m, 50 and 60Hz |
| **Conducted disturbances induced by RF fields** | IEC 61000-4-6 | 6V in ISM + Amateur bands, 3V (0.15-80MHz) |
| **Voltage Dips** | IEC 61000-4-11 | 0 % $U_T$; 0.5 cycle, @ 0°, 45°, 90°, 135°, 180°, 225°, 270° and 315° |
| **Voltage Interruptions** | IEC 61000-4-11 | Interrupt >95% drop, 5s |
| **Radiated Disturbance** | FCC 47 CFR Part 15, Subpart B<br>CISPR 11, Group 1, Class B | |
| **Conducted Disturbance** | CISPR 11, Group 1, Class B | |
| **RF Emissions** | IEC 61000-3-2 Harmonics<br>IEC 61000-3-3 Flicker | |

With the exception of FCC 47 CFR Part 15, all the other standards are normative references of IEC 60601-1-2:2014, Medical electrical equipment – Part 1-2: General

requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances – Requirements and tests and conform to IEC 60601-1-2:2014

The MATRx plus was tested in accordance with IEC 60601-1:2005 (Third Edition) + CORR. 1:2006 +CORR. 2:2007 + A1:2012 and passed the following wireless safety and radio frequency wireless coexistence safety tests:

*Table 2: Wireless Safety and Radio Frequency Wireless Coexistence Safety Tests*

| Basic EMC Standard | | Test Name |
|---|---|---|
| **ETSI EN 300 328 v1.8.1** | **Wireless Safety Test** | Electromagnetic compatibility and Radio spectrum Matters (ERM) |
| **ETSI EN 300 328 v1.8.1** | **Wireless Safety Test** | Wideband transmission systems |
| **ETSI EN 300 328 v1.8.1** | **Wireless Safety Test** | Data transmission equipment operating in the 2,4 GHz ISM band and using wide band modulation techniques |
| **ETSI EN 300 328 v1.8.1** | **Wireless Safety Test** | Harmonized ENcovering the essential requirements of article 3.2 of the R&TTE Directive |
| **ETSI EN 301 489-1 v1.9.2** | **Wireless Safety Test** | Electromagnetic compatibility and Radio spectrum Matters (ERM) |
| **ETSI EN 301 489-1 v1.9.2** | **Wireless Safety Test** | ElectroMagnetic Compatibility (EMC) standard for radio equipment and services; Part 1: Common technical requirements |
| **ETSI EN 301 489-17 v2.2.1** | **Wireless Safety Test** | Electromagnetic compatibility and Radio spectrum Matters (ERM) |
| **ETSI EN 301 489-1 v1.9.2** | **Wireless Safety Test** | ElectroMagnetic Compatibility (EMC) standard for radio equipment Part 17: Specific conditions for Broadband Data Transmission Systems |
| **AAMI TIR69:2017** | **Radio frequency wireless coexistence safety test** | Risk management of radio-frequency wireless coexistence for medical devices and systems |

## MAGNETIC RESONANCE (MR) COMPATIBILITY

The device has not been tested for MRI compatibility and should not be used in the vicinity of an MRI device.

## SOFTWARE

The De Novo request provided adequate software documentation consistent with a "Moderate" level of software concern as discussed in the FDA Guidance Document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices," issued May 11, 2005.

Software validation and verification testing demonstrated that the device met its design, implementation, and cybersecurity requirements.

## HUMAN FACTORS

A human factors assessment was conducted as part of the clinical trial for the MATRx

plus device. Please refer to the 'Summary of Clinical Information' below.

**PERFORMANCE TESTING – CLOSED LOOP ALGORITHM**

The MATRx plus device is considered a Physiological Closed-Loop Controlled (PCLC) medical device. The sponsor has provided a conformity report to the following consensus standard:

IEC 60601-1-10 The General requirements for basic safety and essential performance – Collateral Standard: Requirements for the development of physiologic closed-loop controllers.

The sponsor has adequately addressed the following elements in the closed-loop system :

- Control scheme and method
- Rationale for choice of controller
- Control parameters (e.g., Proportional and Integral (PI) gains)
- Control variables (e.g., infusion rate)
- Controller robustness (i.e., against patient variability).
- Controller stability
- Details of signal processing that enable the feedback system and how different sensors (e.g. oximeter and flow sensor) are combined to inform the positioner controller
- Sensor accuracy variability and potential detrimental effects on the positioner
- Reliability of the sensor in situations that may pose disturbance to the reading (e.g., patient movement)

**PERFORMANCE TESTING – BENCH**

The following testing was reviewed as a part of the bench performance testing:

*Table 3: Bench Performance Testing*

| Test | Test Objectives |
|---|---|
| Mandibular Positioner, Accuracy Data | (i) Device will be able to send a position feedback signal to the controller that reports a new position within 0.5mm of the actual physical position of the trays/mandible; and the accuracy will be maintained under expected clinical loads.<br>(ii) The mandibular positioner will be able to physically endure the use life of the device under normal operating load without failure and maintain the accuracy. Simulated use life testing was conducted based on days of single patient use, movements per patient use, and approximated number of insertion and removal cycles per patient use. This number was extrapolated for the final use life determination, and testing was conducted at this value. |

| | |
|---|---|
| Mandibular Positioner, Force Limit Test | Mandibular positioner will be incapable of applying a force that could induce serious injury under a worst-case fault scenario of 70 Newtons as reported in the literature. This is a force that the average patient should be able to voluntarily counteract by resisting anterior/posterior motion or clenching. The literature supported forces in a range of 150N or more, therefore, a conservative acceptance criteria has been established. |
| Device Force Limitation Simulation | (i) Demonstrate the ability of users to voluntarily stall the mandibular positioner in a fault position (i.e., full stroke speed) (ii) Demonstrate that without voluntary action to resist the force, the trays dislodge from their seated position on the teeth prior to injury or maximum force (i.e., 70N) |
| Impression material breakage | (i) Demonstrate the ability of the impression material used to form the temporary oral appliance to maintain integrity over the use life of the temporary oral appliance |

The data provided showed each test was passed according to its pre-specified acceptance criteria.

## SUMMARY OF CLINICAL INFORMATION

Objective

To evaluate the ability the MATRx plus to safely and effectively identify which patients with obstructive sleep apnea are expected to achieve therapeutic success with oral appliance therapy and to recommend an efficacious target mandibular position at which intraoral therapy may be effective.

Study Design

The clinical study was completed in two phases. Phase I used a prototype of the device and established proof of concept ahead of Phase II. This review focuses on Phase II, as it is pivotal, uses the final finished device, and includes a human factors assessment. The device was used as intended, unattended in the home environment following deployment from a dental professional's office.

Human Factors

Human factors verification and validation testing was also evaluated as part of the pivotal clinical trial. The study provided a human factors assessment as per the FDA Guidance Document "Applying Human Factors and Usability Engineering to Medical Devices" issued February 3, 2016.

As per the guidance, 15 patients were recruited for each study which were conducted in a bedroom environment. Each patient had been previously diagnosed with OSA. Participants and providers were evaluated for comprehension-based tasks.

The human factors evaluation included the following:

- Simulated device set-up of the portal and tablet – device set up, tray fabrication, patient self-insertion of trays, and reprocessing

- Actual use testing- actual patient overnight use, technician reading and understanding the report

Clinical Endpoints

Effectiveness

1. Predictive Accuracy
   Successful treatment with an oral appliance was defined prospectively as achieving an oxygen desaturation index (ODI) with the custom appliance, by the automated analysis of a full night home sleep test, of less than 10 desaturation events per hour. Unsuccessful treatment with an oral appliance was defined as achieving an ODI on the home sleep test greater than or equal to 10 desaturation events per hour.
   - The MATRx plus predictive accuracy endpoint was assigned if the sensitivity and specificity was found to be statistically significant to reject the null hypothesis that sensitivity was $\leq 0.6$
   - A secondary outcome was assigned if the MATRx plus target protrusive position was found to be statistically significant to reject the null hypothesis that target accuracy was $\leq 0.6$

2. Safety
   The pivotal study success criteria are as follows:
   - No significant safety concerns reported by the coordinator, dentist, or participant.
   - Only minor discomfort reported on the MATRx plus post-study device participant questionnaires.
   - No failure of the software that resulted or could result in injury to the participant if it were to recur.
   - No movement beyond full retrusion and maximum protrusion set values.

3. Usability
   - The MATRx plus usability endpoint was assigned if usability testing of the device produced an accurate prediction for oral appliance therapy and effective titration level as demonstrated by actual use testing relating to the set-up, placement, use, and removal of the device by the participant in the home environment

Statistical Methodology

The predictive accuracy endpoint for the study was determined by calculating the sensitivity and specificity of the predictions made from the MATRx plus test, where 95% confidence intervals were obtained using 1-sided binomial calculations, which were sufficient to reject the null hypothesis that sensitivity was $\leq 0.6$. A secondary predictive accuracy outcome was assigned if the MATRx plus target protrusive position was found to be statistically significant, where 95% confidence intervals were obtained using 1-sided binomial test calculations, which were sufficient to reject the null hypothesis that target accuracy was $\leq 0.6$.

Participant Selection

Individuals previously diagnosed with or treated for OSA were recruited for the study. Only the mild to moderate population was used in the final evaluation. The gender distribution, age, and BMI of the study population was representative of the general population of individuals with obstructive sleep apnea.

Inclusion Criteria

1) Aged between 21 and 80 years
2) Obstructive sleep apnea (only mild to moderate OSA patients' data were used)
3) Oxygen Desaturation Index > 10 $hr^{-1}$
4) Body mass index less than 45 $kg/m^2$
5) Neck circumference less than 50 cm
6) Absence of severe oxyhemoglobin desaturation during sleep as indicated by a mean $SaO_2$ value greater than 87%
7) Mandibular range of motion greater than 5 mm
8) Adequate dentition (10 upper and 10 lower teeth)
9) Ability to understand and provide informed consent
10) Ability and willingness to meet the required schedule

Exclusion Criteria

1) Inability to breathe comfortably through the nose
3) Anticipated change in medical therapy that could alter the severity of OSA during the protocol
4) Anticipated change in body weight (5% or more) during the protocol
5) Symptomatic, non-respiratory sleep disorder, e.g., restless leg syndrome or chronic insomnia
6) Severe respiratory disorder(s) other than sleep disordered breathing
7) Loose teeth or advanced periodontal disease
8) Participation in other studies that could interfere with study protocol
9) Pregnant or nursing (added in phase II)
10) Heart failure (added in phase II)
11) Cerebral vascular incident within the last 12 months (added in phase II)
12) Use of pacemaker or other life supporting device (added in phase II)

Study Procedure

Each participant received a two-night baseline, pretreatment, respiratory evaluation in the home using a legally marketed home sleep recorder set to measure 4% oxygen desaturations (Phase I: Snore SAT, K002159; Phase II: MATRx plus, K163665) to determine the presence and severity of obstructive sleep apnea. The baseline study with the Home Sleep Apnea Test was used, in part, to determine eligibility for the MATRx plus study. All baseline data were reviewed by a Sleep Health professional.

Each participant was then evaluated by the dental co-investigator for adequate dentition and other dental criteria. Participants were fitted with upper and lower Titration Trays filled with impression material. The dentist measured the maximum retrusion, normal bite, and protrusion values from the scale on the MATRx plus titration trays. On the first night of the home MATRx plus oral appliance assessment study, the values provided by the dentist for normal bite,

retrusion, and protrusion were entered into the software by a technician and used to control the limits of protrusion.

The participants then performed the MATRx plus OA assessment study over a two- or three-night sequence in their own home with no attendant present. At bedtime, the participant independently applied the nares cannula and the finger oximeter, inserted the trays into the mouth and initiated the study. This included establishing the Bluetooth pairing and connecting the sensors to the device, and wearing a respiratory effort belt. The participant then fell asleep and the device adjusted the position of the mandible in response to changes in detected airflow and oximetry according to the device's control algorithms. The following morning, the participant removed the titration trays and other sensors and terminated the program. The night's data were used by the system to determine the parameters for the subsequent night's settings, for a total of up to six nights.

If any of the study nights were incomplete (i.e., less than 4 hours of usable data) the incomplete study night was repeated if the participant was willing. Post-study, the data were reviewed to verify that the device was set up and used properly. Following each study night, the participant completed a safety-related questionnaire in which additional factors relating to the safety (e.g., ease of applying and removing the trays, pain and discomfort, oral obstruction, tray retention, ability to understand alerts, etc.) was recorded. At the end of the complete study, the participant completed additional questions related to the use of the device (e.g., ease of ending the study, difficulty in positioning trays, overall opinion of the device, ability to understand notifications and instructions, etc.). A coordinator interviewed the participants on the results of the questionnaire. A licensed dentist completed an intraoral exam to inspect for any adverse events. The exam was performed within five days of the study and a separate subjective interview was conducted to gather additional information by the dentist related to dental safety, ease of use, comfort and adverse events.

After the completion of the MATRx plus study, the data were automatically analyzed, and the participants labeled as either: 1) predicted success (responder); or 2) predicted failure (non-responder). If insufficient data on which to base a prediction were attained, i.e., less than four hours of sleep on a study night on the required nights, the participant was labeled inconclusive. The predication was done using a trained binary classifier. The test also provided a predictive target protrusive position for participants labeled as predicted responders Once the target protrusive value was obtained, the protrusion level was transferred to the patient's final oral appliance and was tested as per the sponsor's success criteria with the MATRx Home Sleep Apnea test, which has been validated for using the Oxygen Desaturation Index (ODI).

A successful MATRx plus study was defined as an ODI of less than 10, where ODI is measured as the number of oxygen desaturation events of 4% or greater per hour. If the success criteria were not achieved at the target position, the participant's oral appliance was advanced, and the participant was retested at 1 mm increments from target until the participant was found to be a therapeutic success (ODI < 10) or a clinical protrusive limit was reached.

## Results

Identification of Responders

When considering the mild and moderate sleep apnea population, the sensitivity and Positive Predictive Value (PPV), i.e., the ability of the test to accurately select favorable candidates for oral appliance therapy, and the results of the prediction of oral appliance responders are provided in the table below. Though the specificity and Negative Predictive Value (NPV)were low, the predictive success rate was high (87%). The validity of the test in this population was confirmed by the PPV (i.e., the sensitivity is not attained by incorrectly assigning a prediction of responder to all or a majority of candidates). The overall success rate for the identification of responders was 86.7%.

**Table 4: Association Between the MATRx Plus Test Predication and Outcome of Oral Appliance at Final Protrusion for Individuals with Mild to Moderate Severity Obstructive Sleep Apnea.**

| | Predictive Success Category | Predictive Failure Category |
|---|---|---|
| Successful Identification of Responders | 49 | 3 |
| Failure to Identify Responders | 2 | 6 |

**Table 5: Measure of Accuracy Between the MATRx plus Test Predication and Oral Appliance Outcome at Final Protrusion for Individuals with Mild/Moderate Obstructive Sleep Apnea**

| | % | Lower Confidence Limit | Upper Confidence Limit |
|---|---|---|---|
| Sensitivity | 94.2 | 0.86 | 1.00 |
| Specificity | 75.0 | 0.40 | 1.00 |
| Positive Predictive Value | 96.1 | 0.88 | 1.00 |
| Negative Predictive Value | 66.7 | 0.34 | 1.00 |

Identification of Efficacious Target Protrusion

86.3% of participants were correctly predicted as responders and were successfully provided with an effective target protrusion. Of the remaining participants, 10.0% required an additional adjustment by a titration protocol and 3.9% were determined to be false positives through clinical follow-up.

Of the participants who required additional protrusion, the amount of additional protrusion required ranged from 1 to 4 mm (11.5-33.3% of the patient's maximum protrusion). The median target protrusion provided by the MATRx plus was 66.7% of the patient's maximum protrusion and the median effective protrusion (once titration was completed with the custom oral appliance) was 66.7% of the patient's maximum protrusion.

Safety

The MATRx plus study had no significant safety concerns reported by the coordinator, dentist, or participant. Many of the concerns that were reported were due to patient discomfort and disruptions in sleep. The safety criteria were assessed as follows:

- Temporary discomfort was reported on the MATRx plus post-study device participant questionnaires. Patients reported feeling pain in teeth, joint, and jaw and minor gum irritations, but the pain resolved within a few hours after the device was removed.
- Temporary discomfort was reported on the MATRx plus post-study dental assessment. Patients reported a temporary change in bite and soreness in teeth
- No failure of the software was reported that resulted or could result in injury to the participant if it were to recur.
- No movement beyond full retrusion and maximum protrusion set values were reported.

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

**LABELING**

The labeling (User Instructions) meets the requirements of 21 CFR Part 801.109 for prescription devices.

The Healthcare Provider Manual instructions for use includes the following:

a. The titration study workflow
b. The User Profile is described as the following:
    - As healthcare providers who will be responsible for dispensing the device, instructing the patient, assessing suitability, and prescribing treatment
    - As patients who will be using the prescription home use device for a home sleep study
c. Complete instructions on device components, set-up, dispensing, use instructions, cleaning, disinfection, and storage
d. A description of error messages and alarms
e. Instructions on when to discontinue study
f. Warnings and contraindications
g. Instructions on reviewing patient data and study reports

The Patient Manual instructions for use includes the following:

a. Complete instructions on device components, set-up, use instructions, cleaning, and storage
b. A description of error messages and alarms
c. Instructions on when to discontinue study

d. Warnings and contraindications

**RISKS TO HEALTH**

The table below identifies the risks to health that may be associated with use of the auto titration device for oral appliances and the measures necessary to mitigate these risks.

Table 6: Identified Risks to Health and Mitigation Measures

| **Identified Risk** | **Mitigation Measures** |
|---|---|
| Adverse tissue reaction | Biocompatibility evaluation |
| Infection | Reprocessing validation<br>Labeling |
| Intraoral/TMJ injury, irritation or pain due to:<br>▪ Use error<br>▪ Algorithm-directed positioning<br>▪ Interference with other devices<br>▪ Device electrical failure | Clinical performance testing<br>Human factors assessment<br>Non-clinical performance testing<br>Software verification, validation, and hazard analysis<br>Electrical safety testing<br>Electromagnetic compatibility (EMC) testing<br>Wireless coexistence testing |
| Incorrect titration level due to use error | Human factors assessment<br>Labeling |
| Disruption of sleep | Labeling |
| Temporary change in bite or dentition | Labeling |

**SPECIAL CONTROLS:**

In combination with the general controls of the FD&C Act, the auto titration device for oral appliances is subject to the following special controls:

(1) Clinical performance testing must evaluate the following:
  (i) Performance characteristics of the algorithm; and
  (ii) All adverse events.

(2) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions for use, including the following:
  (i) Validation of the closed loop algorithm;
  (ii) Mechanical integrity over the expected use life;
  (iii) Characterization of maximum force, distance, and speed of device movement; and
  (iv) Movement accuracy of intraoral components.

(3) Performance testing must demonstrate the wireless compatibility, electrical safety, and electromagnetic compatibility of the device in its intended use environment.

(4) Software verification, validation, and hazard analysis must be performed.

(5) The patient-contacting components of the device must be demonstrated to be biocompatible.

(6) Performance data must validate the reprocessing instructions for any reusable components.

(7) Patient labeling must include:
(i) Information on device use, including placement of sensors and mouthpieces;
(ii) A description of all alarms; and
(iii) Instructions for reprocessing any reusable components.

(8) A human factors assessment must evaluate simulated use of the device in a home use setting.

## BENEFIT/RISK DETERMINATION

The known probable risks of the device are based on the data collected in the clinical study described above. The device exhibited an acceptable safety profile in the clinical studies which were conducted, and any adverse events that occurred were temporary and had complete resolution. No device-related serious adverse events were observed, such as swallowing or aspiration of device components, obstruction of oral breathing, or permanent changes in dentition.

As described above, the MATRx plus device consists of a closed loop auto-titration device to be used with a temporary oral appliance to provide information to the healthcare professional regarding a patient's response to oral appliance therapy and a predicted effective titration level for the final oral appliance. Several of the components have been previously used in Zephyr's home sleep apnea test (HSAT). The HSAT device was cleared under K163665, and is regulated as a Breathing Frequency Monitor under 21 CFR 868.2375. The device is to be prescribed and dispensed by a healthcare professional and to be used in a home-use setting. Risks of a harmful event would be related to improper use or device malfunction that may cause tooth, jaw, and joint discomfort, sleep disruption, increased salivation, or tooth movement. All of these risks were seen in the clinical study with the use of the device except for tooth movement, although tooth movement is a common side effect of intraoral devices, even for short durations. The probability of a harmful event with the use of this device is low and any adverse events reported would likely be temporary in nature. If patients cannot tolerate the MATRx plus device, they may simply remove it from their mouth and opt for traditional manual titration using the final oral appliance.

The probable benefits of the device are also based on the data collected in the clinical study described above. The benefit of this device is that it may be used as a tool for the dentists or medical sleep specialists to identify OSA patients who may respond to intraoral appliances. It may also provide a mandible protrusion starting point for the titration process for the final oral appliance. The numerical titration value provided by the device could be used as a starting point to determine an efficacious protrusive position for the patient and then be adjusted accordingly based on clinical expertise of the dentist.

Patient Perspectives

The MATRx plus study collected data on patients diagnosed with mild to moderate obstructive sleep apnea based on the inputs of airflow and oxygen desaturation. The collected data was provided to the healthcare professional and predicted whether the patient may be a responder to oral appliance therapy and if so, to provide a target protrusive level from which to start the titration process in the final oral appliance. The conducted study demonstrated that some patients reported sleep disruptions from use of this device. Sleep disruptions arose from multiple alarms sounding throughout the night, motion of the mandibular positioner trays, noise form the mandibular positioner movement, and general discomfort from wearing the device during sleep. However, sleep disruptions are also common with other devices that use sensors placed on the body overnight while patients are sleeping, such as home sleep apnea tests.

Benefit/Risk Conclusion

In conclusion, given the available information above, the data provide support for identifying whether a patient is a candidate for oral appliance therapy and if so, a possible mandible protrusion position to start the titration process. The data demonstrate that the probable benefits outweigh the probable risks for MATRx plus. The risks can be mitigated by the use of general controls and the identified special controls.

## CONCLUSION

The De Novo request for the MATRx plus is granted and the device is classified under the following:

Product Code: QCJ
Device Type: Auto titration device for oral appliances
Class: II
Regulation: 21 CFR 872.5571